




Patterns of the use of advanced radiation therapy techniques for the management of bone metastases and the associated factors in Victoria

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Abstract

Introduction: To describe the pattern of the use of advanced radiation therapy (RT) techniques, including intensity-modulated RT (IMRT), volumetric modulated arc therapy (VMAT), and stereotactic body RT (SBRT) for the management of bone metastases (BM), and the associated factors in Victoria.

Methods: We used a population-based cohort of patients from the state-wide Victorian Radiotherapy Minimum Data Set (VRMDS) who received RT for BM between 2012 and 2017. The primary outcome was proportion of RT courses using advanced RT techniques. The Cochran-Armitage test for trend was used to evaluate temporal trend in advanced RT use. Multinomial logistic regression was used to identify factors associated with advanced RT use.

Results: A total of 18,158 courses of RT were delivered to 10,956 patients—16,626 (91.6%) courses were 3D conformal RT, 857 (4.7%) IMRT/VMAT and 675 (3.7%) SBRT. There was a sharp increase in IMRT/VMAT use from <1% in 2012–2015, to 10.1% in 2016 and 16.3% in 2017 (P -trend < 0.001). Increase in SBRT use was more gradual, from 1.2% in 2012 to 4.8% in 2016 and 5.5% in 2017 for SBRT (P -trend < 0.001). In multivariate analyses, year of RT was the strongest predictor of IMRT/VMAT use (OR = 41; 95%CI = 25–67; P < 0.001, comparing 2012–2013 and 2016–2017). Primary tumour type (prostate cancer) was the strongest predictor of SBRT use (OR = 6.07; 95% CI = 4.19–8.80; P < 0.001).

Conclusion: Overall, there was increasing trend in the use of advanced RT techniques for BM in Victoria, with a distinct pattern for IMRT/VMAT compared with SBRT – SBRT uptake was more gradual while IMRT/VMAT uptake was abrupt, occurring contemporaneously with Medicare Benefit Scheme funding changes in 2016.

Key words: bone metastases; IMRT; radiation therapy; stereotactic; VMAT.

Introduction

Palliative radiation therapy (RT) is a well-established treatment modality for the management of bone

metastases (BM), to reduce pain, preserve function and reduce the risk of pathologic fractures.¹ RT techniques and technologies continue to evolve rapidly. While three-dimensional conformal radiation therapy (3DCRT) is

currently still the most commonly employed RT technique, advanced RT techniques such as intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT) and stereotactic body radiation therapy (SBRT) are becoming more common.

These advanced RT techniques offer more conformal RT plans – better tumour coverage and reduced dose to neighbouring organs at risk – and IMRT/VMAT are the current standards of care, in *curative* setting, for many tumour sites such as head and neck² and prostate cancers.³ The use of SBRT, which involves delivery of ablative radiation doses with a very small margin of surrounding tissues, is also increasingly used in curative setting for tumour such as lung cancer.⁴ However, these advanced RT techniques are significantly more resource-intensive than 3DCRT, requiring longer time from RT planning to treatment delivery, more extensive physics quality assurance (QA) checks and more robust on-treatment verification and treatment time. In January 2016, new Medical Benefits Scheme (MBS) items were introduced to differentiate these advanced RT techniques from 3DCRT (Table 1), with increased reimbursement to account for the complexity in RT planning, delivery and treatment verification of those advanced RT techniques.⁵

Table 1. MBS reimbursement for different radiation therapy techniques and number of fractions for bone metastases

Component of RT	MBS item number	MBS payment per item	Total MBS payment
3DCRT			
CT simulation	15550	AUD 594.50	AUD 1320.35–
RT planning	15556	AUD 600.50	AUD 1948.80
(depending on number of PTV and OAR)	15559	AUD 808.90	for 1 fraction;
	15562	AUD 1071.10	AUD 1821.75–
Treatment delivery	15257	AUD 52.30 (per fraction)	AUD 2947.35 for 5 fractions;
Treatment additional fields (up to 5 fields)	15272	AUD 32.75 (per field, per fraction)	AUD 2448.50–
Treatment verification	15700	AUD 40.30 (per fraction)	AUD 4497.60 for 10 fractions
IMRT/VMAT/SBRT			
CT simulation	15555	AUD 648.05	AUD 4208.25
RT planning	15565	AUD 3332.65	for 1 fraction;
Treatment delivery	15275	AUD 160.40 (per fraction)	AUD 5118.45 for 5 fractions;
Treatment verification	15715	AUD 67.15 (per fraction)	AUD 6256.20 for 10 fractions

3DCRT, three-dimensional conformal radiation therapy; CT, computed tomography; IMRT, intensity-modulated radiation therapy; MBS, Medicare Benefit Scheme; OAR, organs at risk; PTV, planning target volume; SBRT, stereotactic body radiation therapy; VMAT, volumetric modulated arc therapy.

The aim of this study was to describe the changing pattern of the use of advanced RT techniques, in particular IMRT/VMAT and SBRT for the palliative management of BM in Victoria, and to identify factors associated with advanced RT techniques use.

Methods

Study population

The study comprised a population-based cohort of patients with solid tumours who received RT for BM between 2012 and 2017, captured in the Victorian Radiotherapy Minimum Data Set (VRMDS). The VRMDS is administered by the Victorian Department of Health, collecting demographic, administrative and clinical data for all patients who received RT in both the public and private sectors in Victoria. For this study, we included only RT courses where the target site was documented as bone, and patients with primary bone malignancies (ICD-10 code: C40–C41) were excluded.

Primary outcomes and covariables

The primary outcome of the study was the proportion of RT courses for BM, categorized as ‘palliative’ by the provider, using ‘advanced RT techniques’, defined as IMRT/VMAT or SBRT. IMRT and VMAT were grouped together in the VRMDS, and it was not possible to differentiate the two techniques. Factors associated with the use of advanced RT techniques that were evaluated included: patients’ age at time of treatment, sex, primary cancer type, site of BM, socioeconomic status, geographic remoteness of area of residence, treatment institution type (public vs private) and location (metropolitan vs. regional). Socioeconomic status was derived from residential postcode using the Socio-Economic Indexes for Areas (SEIFA) index for relative socioeconomic disadvantage based on the Australian Bureau of Statistics data and was subdivided into quintiles based on the Victorian general population. Patients’ area of residence was classified as major city, inner regional, outer regional, remote or very remote using the Australian Statistical Geographical Standard (ASGS) remoteness structure.

Statistical analyses

Descriptive statistics were used to describe the frequencies and percentages for categorical variables; and mean and standard deviation (SD), or median and interquartile (IQR) as appropriate, for continuous variables. Differences in characteristics of patients who had advanced RT techniques versus 3DCRT were evaluated using the Pearson’s χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables. The Cochran-Armitage test for trend was used to evaluate temporal trend for advanced RT techniques use.

Multinomial logistic regression analysis was used to evaluate factors associated with advanced RT techniques use, with 3DCRT considered as the reference outcome category. Variables with $P < 0.1$ in univariable analyses were included in the multivariable modelling. All multivariate modelling employed the robust standard errors, with analyses clustered on patient identifiers to allow for clustering of patients who had multiple courses of RT. To account for multiple testing, a 2-sided P -value of <0.005 was considered statistically significant. All statistical analyses were performed using Stata/SE 17 (StataCorp, College Station, TX).

Results

A total of 10,956 patients received 18,158 courses of palliative RT for BM. Of these, 16,626 (91.6%) courses were delivered with 3DCRT, and 1,532 courses were delivered using advanced RT techniques—857 IMRT/VMAT (4.7%) and 675 SBRT (3.7%) (Table 2). The most common site of RT was to the spine (49%), and the most common primary cancer types were lung cancer (23.9%) and prostate cancer (23.8%) (Table 2).

Advanced RT techniques (IMRT/VMAT or SBRT) were more likely to be used in men, especially for SBRT (5% in men vs. 2% in women, $P < 0.001$). There was a higher proportion of SBRT techniques use for BM in prostate cancer (8.9%) compared with other cancers ($P < 0.001$). Advanced RT techniques were more commonly used for treatment of BM in the pelvis (10% IMRT/VMAT and 10% SBRT) compared with other sites of BM ($P < 0.001$). The median number of fractions delivered with IMRT/VMAT was also higher compared with 3DCRT ($P < 0.001$).

Patients from the highest socioeconomic quintile (10.3%) and those who lived in major cities (9.4%) were more likely to be treated with advanced RT techniques ($P < 0.001$). Advanced RT techniques for BM were more commonly delivered in private institutions (9.3% IMRT/VMAT and 7.3% SBRT) and metropolitan institutions (5.0% IMRT/VMAT and 4.8% SBRT), compared with public institutions (1.7% IMRT/VMAT and 1.4% SBRT) and regional institutions (3.9% IMRT/VMAT and 0.02% SBRT) ($P < 0.001$) (Table 2). Patients from inner regional, outer regional, remote or very remote areas who had treatment in metropolitan centres were equally likely to be treated with advanced RT techniques such as SBRT compared to those from major cities; however, those treated in regional centres were less likely to be treated with advanced RT techniques (Table 3).

There was a marked increase in advanced RT techniques use for BM over time—from 0.2% in 2012 to 16.3% in 2017 for IMRT/VMAT, and from 1.2% in 2012 to 5.5% in 2017 for SBRT (P -trend <0.001). There was an increasing use of advanced RT techniques across all age categories (Fig. 1a and 2a) and both sexes (Fig. 1b

Table 2. Variables associated with the use of advanced radiation therapy techniques

	3DCRT 16626 (92.6%)	IMRT/VMAT 857 (4.7%)	SBRT 675 (3.7%)
Age at radiation therapy			
Mean (SD)	68.4 (13.2)	69.8 (13.1)	67.2 (10.5)
<60	4,012 (92.4%)	188 (4.3%)	141 (3.3%)
60–69	4,535 (90.6%)	211 (4.2%)	259 (5.2%)
70–79	4,821 (91.4%)	238 (4.5%)	216 (4.1%)
≥80	3,258 (92.1%)	220 (6.2%)	59 (1.7%)
Sex			
Male	9,728 (91.4%)	501 (4.7%)	535 (5.0%)
Female	6,898 (93.3%)	356 (4.8%)	140 (1.9%)
Primary cancer			
Lung	4,118 (95.0%)	145 (3.3%)	72 (1.7%)
Prostate	3,709 (85.8%)	229 (5.3%)	386 (8.9%)
Breast	3,177 (91.9%)	221 (6.4%)	60 (1.7%)
Gastrointestinal	1,700 (92.4%)	108 (5.9%)	32 (1.7%)
Melanoma	859 (94.2%)	18 (2.0%)	35 (3.8%)
Others	3,063 (93.1%)	136 (4.1%)	90 (2.7%)
Target site of radiation therapy			
Spine	8,125 (91.7%)	459 (5.2%)	277 (3.1%)
Skull	1,748 (95.6%)	23 (1.3%)	58 (3.2%)
Rib	1,192 (91.6%)	37 (2.8%)	72 (5.5%)
Shoulder	779 (94.9%)	26 (3.2%)	16 (2.0%)
Hip	972 (94.1%)	50 (4.8%)	11 (1.1%)
Pelvis	1,135 (79.8%)	145 (10.2%)	142 (10.0%)
Extremities	1,281 (97.4%)	26 (2.0%)	8 (0.6%)
Multiple sites	1,394 (88.5%)	91 (10.6%)	91 (5.8%)
Number of fractions, median (IQR)	5.0 (5.0, 10.0)	10.0 (5.0, 10.0)	5.0 (3.0, 10.0)
Socioeconomic status			
First quintile (most disadvantaged)	3,471 (93.8%)	151 (4.1%)	80 (2.2%)
Second quintile	2,669 (92.7%)	119 (4.1%)	91 (3.2%)
Third quintile	3,051 (91.9%)	166 (5.0%)	102 (3.1%)
Fourth quintile	3,361 (90.4%)	226 (6.1%)	130 (3.5%)
Fifth quintile (least disadvantaged)	4,074 (89.7%)	195 (4.3%)	272 (6.0%)
Remoteness of residence			
Major cities	11,434 (90.7%)	651 (5.2%)	528 (4.2%)
Inner regional	4,266 (93.3%)	188 (4.1%)	119 (2.6%)
Outer regional/remote/very remote	926 (95.3%)	18 (1.9%)	28 (2.9%)
Treatment institution type			
Public	10,663 (96.9%)	191 (1.7%)	152 (1.4%)
Private	5,963 (83.4%)	666 (9.3%)	523 (7.3%)
Treatment institution location			
Metropolitan	12,627 (90.2%)	696 (5.0%)	674 (4.8%)
Regional	3,999 (96.1%)	161 (3.9%)	1 (0.02%)
Year of RT			
2012	2,486 (98.6%)	6 (0.2%)	29 (1.2%)
2013	3,027 (97.6%)	18 (0.6%)	57 (1.8%)
2014	3,094 (94.9%)	26 (0.8%)	140 (4.3%)
2015	3,106 (95.0%)	21 (0.6%)	141 (4.3%)
2016*	2,655 (85.1%)	316 (10.1%)	150 (4.8%)
2017*	2,258 (78.2%)	470 (16.3%)	158 (5.5%)

*Post changes in Medicare Benefit Scheme funding.

3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; SBRT, stereotactic body radiation therapy; VMAT, volumetric modulated arc therapy.

Table 3. Use of advanced radiation therapy techniques, stratified by remoteness of residence and location of treatment centres

Remoteness of residence	Treatment centre	Number of RT courses	3DCRT	IMRT/VMAT	SRT
Major city	Metropolitan	11,749 (93%)	10,587 (90%)	634 (5.4%)	528 (4.5%)
	Regional	864 (7%)	847 (98%)	17 (2%)	0 (0%)
Inner regional	Metropolitan	1,789 (39%)	1,614 (90%)	56 (3%)	119 (7%)
	Regional	2,784 (61%)	2,652 (95%)	132 (4.7%)	0 (0%)
Outer regional/remote/very remote	Metropolitan	459 (47%)	426 (93%)	6 (1%)	27 (6%)
	Regional	513 (53%)	500 (97%)	12 (2%)	1 (0.2%)

and 2b). While there was an increasing use of IMRT/VMAT for BM in all cancer types (Fig. 1c), the most rapid and early increase in SBRT use was observed in prostate cancer, with more than 10% of prostate cancer BM treated with SBRT by 2014 onwards (Fig. 2c). There was increase in IMRT/VMAT techniques use for all sites of BM (Fig. 1d), but more marked rises in SBRT use were observed in RT for pelvic and rib BM (Fig. 2d). There was increase in IMRT/VMAT and SBRT techniques use over time, when stratified by socioeconomic status and remoteness of residence (Fig. 1e, f, 2e, and f). When stratified by treatment institution, the most marked increases in both IMRT/VMAT and SBRT use were observed in private and metropolitan institutions (Fig. 1g and 2g).

In multivariable analyses, year of treatment was the strongest predictor for IMRT/VMAT techniques use—RT courses delivered in 2016–2017 were 40 times (95% CI = 25–67; $P < 0.001$) more likely to be treated with IMRT/VMAT techniques, compared with treatment delivered in 2012–2013. Other factors associated with increased likelihood of IMRT/VMAT use were cancer type (breast cancer), site of BM (pelvis), remoteness of residency (major cities) and treatment centre (private and regional) (Table 4). The factor most strongly associated with SBRT use was primary cancer type—RT for prostate cancer BM was 6.1 times (95%CI = 4.2–8.8; $P < 0.001$) more likely to be treated with SBRT compared with lung cancer BM. Other factors associated with increased likelihood of SBRT use were younger age, site of BM (pelvis, skull and rib), higher socioeconomic status and treatment institution (private and metropolitan) (Table 4)

Discussion

To the best of our knowledge, this is the only Australian study evaluating the changing pattern in the use of advanced RT techniques, separately for IMRT/VMAT and SBRT, for the palliative management of BM since the change in MBS reimbursement in 2016. We used the state-wide administrative data for over 18,000 courses of RT for BM delivered between 2012 and 2017 in Victoria, and a major strength of this study is that it is based on actual delivered RT data and hence reflects true state-wide patterns of practice in Victoria.

There are only a few population-based studies that have evaluated the use of advanced RT techniques for BM.^{6,7} In a study using the US Medicare claim data for the period between 2011 and 2014, Logan et al reported the use of IMRT and SBRT to be 6% and 4% respectively.⁷ In a separate Canadian study in British Columbia between 2009 and 2016, Chan et al reported a much lower use of IMRT and SBRT, of 0.7% and 0.1% respectively.⁶ They also reported an increase in the use of advanced RT techniques over the study period.⁶ The magnitude of increase in the Canadian study, however, is markedly less than that observed in our study despite covering a similar study period—from 0% in 2009 to 2% in 2016 for IMRT, and 0% in 2009 to 0.4% in 2016 for SBRT.⁶

We identified several factors to be associated with advanced RT techniques use for BM in our cohort. We observed differences in SBRT use between *men* and *women*; however, this is confounded by the higher proportion of SBRT use for prostate cancer, and the difference between men and women was no longer significant in multivariate analyses. Prostate cancer was in fact the strongest predictor of SBRT use. The higher utilization of SBRT for BM in prostate cancer is most likely related to the relatively long natural history and good prognosis in prostate cancer, with good systemic therapy options. There also appears to be much earlier adoption of SBRT for BM in prostate cancer from 2013 onwards (Fig. 2c). This may also have been partly driven by recruitment of men into the Phase 2 POPSTAR study between 2013 and 2014, of which approximately two-thirds of the SBRT sites were BM.⁸

We also observed variation in advanced RT techniques use by *sociodemographic factors*. While patients from regional and remote areas were less likely to be treated with IMRT/VMAT techniques, there were no significant differences in the use of SBRT (Table 4), as these patients likely have access to SBRT at metropolitan centres (Table 3). Patients from the highest socioeconomic quintile were more likely to receive SBRT compared to those from the lowest socioeconomic quintile. Should the emerging data continue to be encouraging for the utilization of SBRT, the adoption of strategies at both provider and government levels will be essential to ensure equal and easy access to SBRT for all cancer patients.

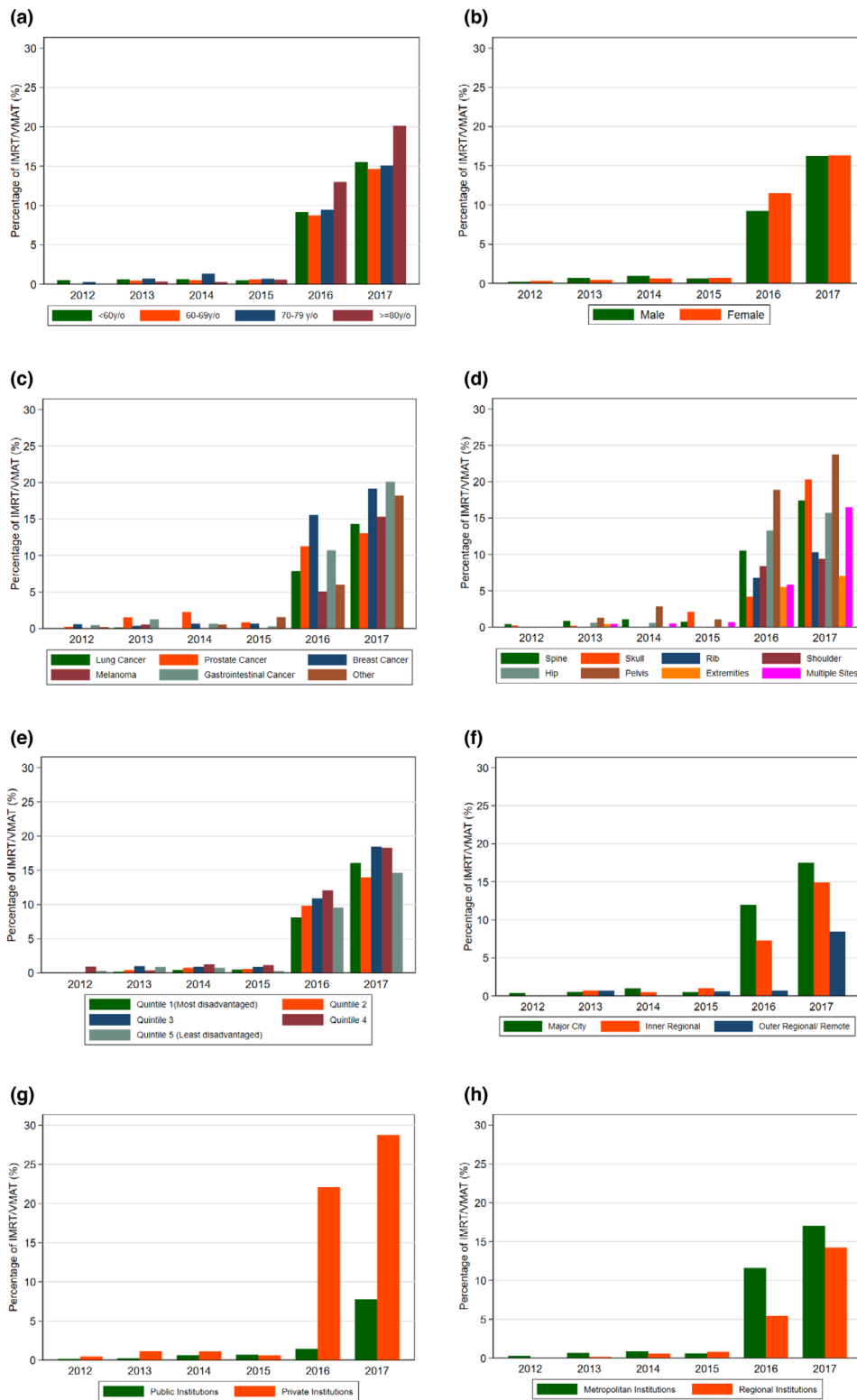


Fig. 1. Use of intensity-modulated RT (IMRT)/volumetric modulated arc therapy (VMAT) techniques for bone metastases over time, stratified by (a) age, (b) sex, (c) primary cancer, (d) target site of radiation therapy, (e) socioeconomic status, (f) remoteness of residency, (g) institution type and (h) institution location.

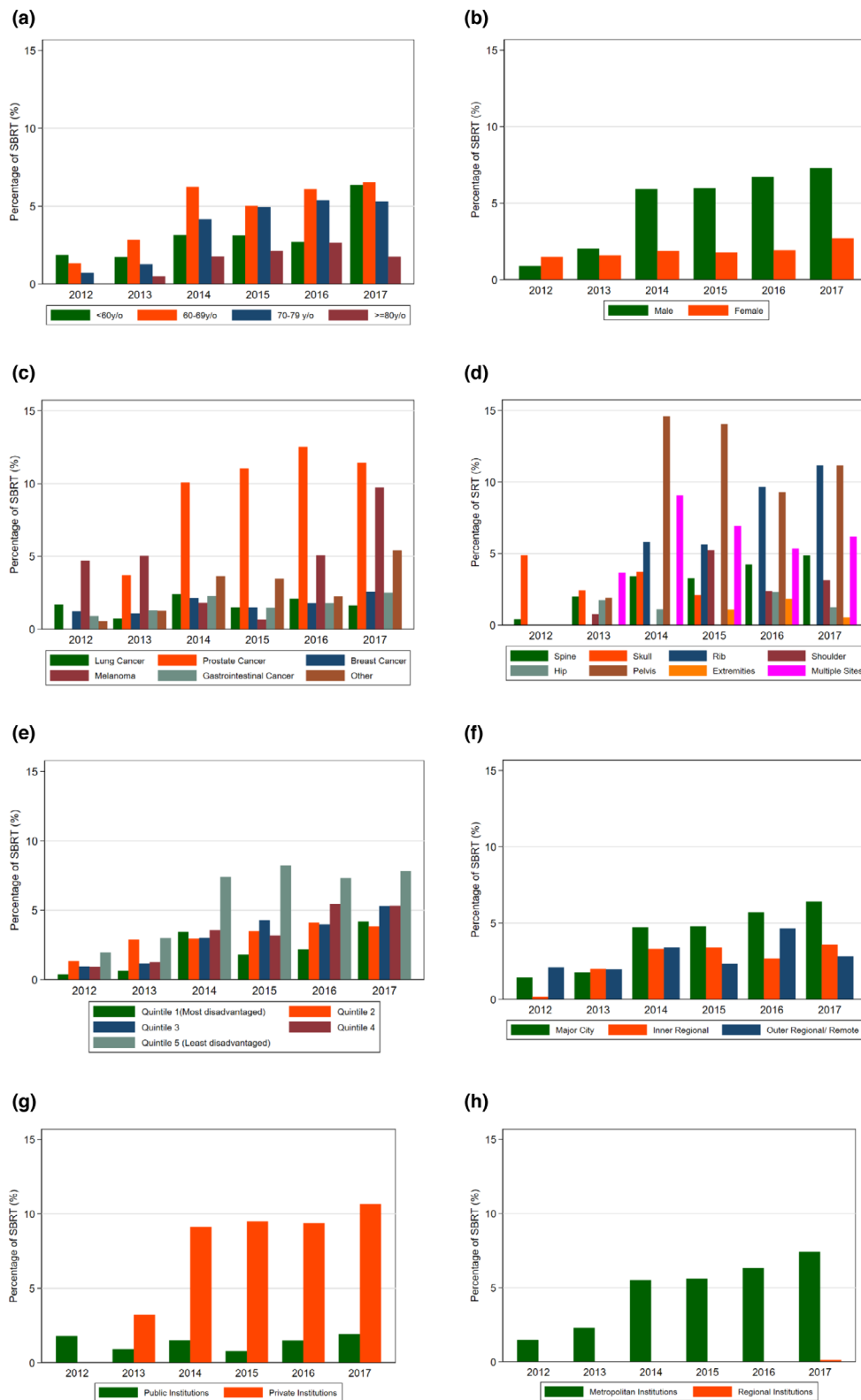


Fig. 2. Use of stereotactic body radiation therapy (SBRT) for bone metastases over time, stratified by (a) age, (b) sex, (c) primary cancer, (d) target site of radiation therapy, (e) socioeconomic status, (f) remoteness of residency, (g) institution type and (h) institution location.

Table 4. Multinomial logistic regression model for association with advanced radiation therapy techniques use (3DCRT techniques was used as reference group)

	IMRT/VMAT		SBRT	
	RRR (95% CI)	P-value	RRR (95% CI)	P-value
Age at radiation therapy				
<60	1		1	
60–69	0.94 (0.71–1.23)	0.63	0.94 (0.71–1.26)	0.69
70–79	0.92 (0.70–1.20)	0.53	0.58 (0.43–0.78)	<0.001
≥80	1.09 (0.79–1.51)	0.58	0.18 (0.11–0.29)	<0.001
Sex				
Male	1		1	
Female	0.88 (0.65–1.18)	0.39	0.81 (0.57–1.14)	0.22
Primary cancer				
Lung	1		1	
Prostate	1.03 (0.72–1.47)	0.87	6.07 (4.19–8.80)	<0.001
Breast	1.64 (1.16–2.33)	0.005	1.00 (0.63–1.59)	0.99
Gastrointestinal	1.32 (0.94–1.87)	0.11	0.93 (0.55–1.55)	0.77
Melanoma	1.14 (0.56–2.29)	0.72	2.84 (1.62–4.98)	<0.001
Others	1.17 (0.83–1.68)	0.38	1.74 (1.16–2.60)	0.008
Target site of radiation therapy				
Spine	1		1	
Skull	0.99 (0.5–1.64)	0.96	2.23 (1.52–3.27)	<0.001
Rib	0.57 (0.37–0.87)	0.009	1.75 (1.26–2.43)	0.001
Shoulder	0.59 (0.37–0.94)	0.025	0.52 (0.29–0.93)	0.028
Hip	0.81 (0.57–1.16)	0.26	0.31 (0.15–0.62)	0.001
Pelvis	1.81 (1.41–2.33)	<0.001	2.21 (1.71–2.86)	<0.001
Extremities	0.28 (0.18–0.45)	<0.001	0.20 (0.09–0.44)	<0.001
Multiple sites	0.74 (0.54–1.01)	0.057	1.56 (1.17–2.09)	0.003
Socioeconomic status				
First quintile (most disadvantaged)	1		1	
Second quintile	0.81 (0.57–1.17)	0.26	1.01 (0.65–1.57)	0.98
Third quintile	0.97 (0.69–1.36)	0.84	1.11 (0.74–1.68)	0.62
Fourth quintile	0.82 (0.60–1.13)	0.22	0.97 (0.65–1.43)	0.87
Fifth quintile (least disadvantaged)	0.72 (0.52–1.00)	0.052	1.76 (1.23–2.51)	0.002
Remoteness of residence				
Major cities	1		1	
Inner regional	0.53 (0.40–0.70)	<0.001	1.06 (0.77–1.45)	0.72
Outer regional/remote/very remote	0.21 (0.10–0.41)	<0.001	1.13 (0.66–1.94)	0.65
Treatment institution type				
Public	1		1	
Private	8.96 (7.17–11.20)	<0.001	4.34 (3.45–5.46)	<0.001
Treatment institution location				
Metropolitan	1		1	
Regional	2.34 (1.78–3.06)	<0.001	0.01 (0.001–0.06)	<0.001
Year of RT				
2012–2013	1		1	
2014–2015	1.75 (0.99–3.09)	0.054	2.86 (2.14–3.84)	<0.001
2016–2017*	41.31 (25.32–67.39)	<0.001	4.53 (3.36–6.10)	<0.001

*Post changes in Medicare Benefit Scheme funding.

3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; RRR, relative risk ratio; SBRT, stereotactic body radiation therapy; VMAT, volumetric modulated arc therapy.

The disparities in advanced RT techniques use were also observed across different *institutional types and locations*. It is likely that some institutions were earlier adopters of advanced RT techniques and would have had experience in implementing these techniques in the curative setting for multiple tumour sites and hence may

have the capacity to transfer of these techniques more easily into palliative management of BM. With increasing institutional experience and streamlined workflow, the resources and time required for advanced RT treatment planning and delivery could be significantly reduced, such that the routine use of advanced RT techniques for

Table 5. Published randomized trials on the use of advanced radiation therapy techniques for management of painful bone metastases

	Study period and country	Study design and population	<i>n</i>	Treatment arms	Primary endpoint definition	Findings
IMRT						
	Sprave, 2018 (IRON-1)	2016–2017 Germany	single institutional, patients with painful spinal metastases	60	CRT: 30Gy/10# (<i>n</i> = 30) IMRT: 30Gy/10# (<i>n</i> = 30)	Radiation-induced toxicity (based on CTCAEv4.03) at 3 months CRT: 4 with G3 tox IMRT: 1 with G3 tox
SRT						
	Sprave, 2018	2014–2017 Germany	Phase 2, single institutional, patients with painful previously untreated spinal metastases	55	CRT: 30Gy/10# (<i>n</i> = 28) SRT: 24Gy/1# (<i>n</i> = 27)	Pain relief (i.e. VAS = 0, or ≥ 2 -point drop on VAS) at 3 months 48% in CRT arm 70% in SRT arm (<i>P</i> = 0.13)
	Ryu, 2019 (NRG/ RTOG0631)	2009–2018 US	Phase 3, multi-institutional, 1–3 sites of spine metastases	339	CRT: 8Gy/1# (<i>n</i> = 130) SRT: 16–18Gy/1# (<i>n</i> = 209)	Pain control (i.e. 3-point improvement on numerical rating pain scale) at 3 months 56% in CRT arm 40% in SRT arm (<i>P</i> = 0.9)
	Nguyen, 2019	2014–2018 US	Phase 2, single institutional, patients with painful bone metastases	160	CRT: 30Gy/10# (<i>n</i> = 79) SRT: 12–16Gy/1# (<i>n</i> = 81)	Pain response[#] (including complete response (i.e. score 0 on VAS and no increase in analgesia) and partial response (i.e. ≥ 2 -point drop on VAS and no increase in analgesia)) 49% in CRT arm 72% in SRT arm (<i>P</i> = 0.03) (at 3 months)
	Pielkenrood, 2021 (VERTICAL trial)	2015–2019 Netherlands	Phase 2, single institutional, patients with bone metastases	89	CRT: 8Gy/1#, or 20Gy/5#, or 30Gy/10# (<i>n</i> = 44) SRT: 18Gy/1#, 30Gy/3#, or 35Gy/5# (<i>n</i> = 45)	Pain response (including complete response (score 0 on BPI and no increase in analgesia) and partial response (i.e. ≥ 2 -point drop in BPI score or decrease in 25% of analgesia use)) at 3 months 32% in CRT arm 40% in SRT arm (<i>P</i> = 0.42)
	Sahgal, 2021 (SC24 / TROG1706)	2016–2019 Canada and Australia	Phase 2/3, multi-institutional, patients with painful spinal metastases	229	CRT: 20Gy/5# (<i>n</i> = 115) SRT 24Gy/2# (<i>n</i> = 114)	Complete pain response (i.e. pain score of 0 on BPI and no increase in analgesia use) at 3 months 14% in 3DCRT arm 35% in SRT arm (<i>P</i> = 0.0002)

BPI, Brief Pain Inventory; CRT, conformal radiation therapy; IMRT, intensity-modulated radiation therapy; SRT, stereotactic radiation therapy; VAS, Visual Analogue Scale. #time point not specified for primary endpoint.

palliative management of BM may be cost-effective. In fact, the cost-utility analyses of the SABR-COMET study showed that SBRT is cost-effective in patients with 1–5 oligometastases, compared with standard of care which include 3DCRT palliative RT in the Canadian healthcare system.⁹

While there was an overall increasing trend in adoption of advanced RT techniques over time, it is important to highlight the distinct differences in the trend for IMRT/VMAT compared with SBRT (Fig. 1 vs. Fig. 2). There appears to be a more gradual increase in SBRT use over the study period, correlating with increasing interest and the emerging evidence on the role of SBRT for local control¹⁰ and symptom control^{11–15} (Table 5). This also corresponds to the period when there were multiple recruiting SBRT trials for BM in Victoria, including the local single-institutional POPSTAR trial for metastatic prostate cancer⁸ and BOSTON trial for metastatic breast

cancer,¹⁶ as well as international trials, which several Victorian institutions contributed to, such as SABR-COMET, SC24/TROG1706 and CORE trials.^{15,17,18} Hence, there is likely an increase in institutional experience in implementing SBRT for BM over our study period and offering SBRT for BM outside of clinical trial setting.

The increase in adoption of IMRT/VMAT, however, appears much more abrupt, with an unequivocal sharp increase from 2016 onwards (Fig. 1)—the year of treatment was in fact the strongest factor associated with IMRT/VMAT use. It is important to acknowledge that there are many factors that may contribute to this observed change in practice, some of which may not have been accounted for in our analyses. There is the indubitable dosimetric advantage of IMRT/VMAT over 3DCRT, but this may be more relevant in the curative setting, with much higher doses.^{2,3} There is however extremely limited, if any, evidence that this dosimetric

advantage translates into meaningful clinical benefits in the *palliative* setting. There is the theoretical advantage in reducing dose and irradiated volume of the surrounding normal tissues, but this will only have practical and meaningful effect for patients in certain situations, e.g. in patients with relatively good prognosis whereby we anticipate the likelihood of re-irradiation in the future. The proportion of this category of patients is unlikely to have increased dramatically in 2016. One thing, however, did not increase over the study period – published high-quality evidence demonstrating clinical benefits of palliative management of BM with IMRT/VMAT. To date, there has been only one single-institutional explorative pilot trial in Germany comparing IMRT and 3DCRT for management of BM in 60 patients, and this was published in 2018,^{19,20} and so, this is unlikely to have impacted on the practice in Australia 2 years earlier.

A seminal event occurring contemporaneously with the unequivocal sharp increase in IMRT/VMAT use was a change in MBS funding in January 2016, which provided increase in funding for advanced RT techniques compared with simpler 3DCRT (Table 1), which may have contributed to the observed change in practice. There has been an earlier example that MBS funding may have influenced RT practice in the management of BM – there is continued underutilization of single-fraction 3DCRT in Australia,^{21,22} given the remuneration disincentive for its use (Table 1). This is despite multiple randomized trials and meta-analyses consistently showing that single-fraction 3DCRT and multi-fraction 3DCRT provide equally effective symptom control for uncomplicated BM¹ and the Royal Australian and New Zealand College of Radiologists Choosing Wisely® recommendations advising against extended fractionation scheme for palliative RT for BM. It is often overlooked that the fee-for-service model also applies in public institutions, and that practice in public institutions may also be influenced by the current reimbursement model.

One of the inherent limitations of population-based administrative datasets, such as the VRMDS, is the lack of granularity to allow for the evaluation of the appropriateness of advanced RT techniques use in each clinical situation. There are situations, in palliative setting, where the use of advanced RT techniques is clinically appropriate and completely justified. For example, there are clear dosimetric benefits in the re-irradiation setting in being able to spare the neighbouring critical organs at risk with advanced RT techniques, or in patients with oligometastatic BM whereby SBRT has been shown to improve OS.¹⁷ There was also lack of clinical information for us to differentiate between uncomplicated and complicated BM (i.e. those with impending or existing pathologic fractures, spinal cord or cauda equina compression). The VRMDS is dependent on coding and reporting by individual institutions, and we could not discount the possibilities of coding errors leading to misclassification of the variables, e.g. the miscoding of

target sites of treatment or systematic miscoding of RT techniques by institutions.

Conclusion

In this study, we observed a marked increase in advanced RT techniques use for palliative management of BM in this large population-based cohort of cancer patients in Victoria. There are distinct secular trends of the increasing use of SBRT; in contrast, the increasing use of IMRT/VMAT has a 'break point' in 2016, with new federal government funding classifications increasing reimbursement for IMRT/VMAT occurring once during this time series. As a technology-driven specialty, we will likely observe the increasing use of advanced RT techniques for BM in the coming years. In our enthusiasm to embrace the use of advanced RT techniques, we need to ensure that our practice is evidence-based and clinically justifiable, to avoid unwarranted disparity in care and suboptimal utilization of healthcare resources. We believe that the observed increase in adoption of IMRT/VMAT techniques in the palliative management of BM has likely occurred ahead of any clinically important patient benefits being established by high-level evidence. On the other hand, as high-level evidence on the benefits of SBRT continues to emerge, developing and refining frameworks such as the Assessment of New Radiation Oncology Technology and Treatments (ANROTAT)^{23–25} will be useful to allow for thoughtful evaluation of these advanced RT techniques for specific clinical indications. This, along with future research, is required to allow for better selection of patients who may truly benefit from the use of IMRT/VMAT/SBRT for BM in the palliative setting, thus ensuring that the funding is aligned with proven patient benefits.

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Data availability statement

Data available on request from the authors.

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